Antimicrobial Resistance Problems in a University Hospital

Uchenna Chinedu Ozumba, FMCPATH
Enugu, Nigeria

Background: The resistance of bacteria to antibiotics, particularly those used for first-line therapy, is an increasing cause for concern. Unfortunately, in Nigeria, much of the antibiotic therapy is not laboratory individualized or even laboratory extrapolated, leading to empirical prescription.

Objective: To determine the prevalence of antibiotic resistance among common pathogens in the University of Nigeria Teaching Hospital (Enugu, Nigeria) and to proffer solutions that will help decrease the prevalence.

Materials and Methods: All clinical isolates, which were isolated by routine methods from routine specimens, sent to the microbiology department had their antibiotic sensitivity performed on sensitivity test agar (Biotec, United Kingdom) using the disc diffusion method in accordance with the National Committee for Clinical Laboratory Standards.

Results: Most of the *Staphylococcus aureus* and coagulase-negative staphylococci were resistant to common antistaphylococcal drugs. Sixty-four percent of the coliforms were multidrug resistant. A similar pattern was observed for *Pseudomonas aeruginosa*. With regards to nonurinary isolates of coliforms, higher rates of resistance were noticed to ampicillin, gentamycin, colistin and ciprofloxacin when compared to urinary isolates.

Conclusion: There is a need for a continuous surveillance program of resistant bacteria to provide the basis for empirical therapy. At the same time, continued adherence to antibiotic policy and procedures in preventing cross-infection is important in the control of antimicrobial resistant bacteria.

Key words: antimicrobial resistance ■ antibiotic policy ■ empirical prescription

 From the Department of Medical Microbiology, University of Nigeria Teaching Hospital, Enugu, Nigeria. Send correspondence and reprint requests for *J Natl Med Assoc.* 2005;97:1714–1718 to: Uchenna Chinedu Ozumba, FMCPATH, Department of Medical Microbiology, University of Nigeria Teaching Hospital, Enugu, Nigeria; e-mail: zumeco@yahoo.com

INTRODUCTION

Since the introduction of antibiotics into clinical use, bacteria have protected themselves by developing antibiotic resistance mechanisms.[1] Multiresistant organisms are diminishing our ability to treat and control the spread of infections.[2] Resistance to antibiotics has undermined the idealistic hope that bacterial infection would cease to be an important cause of death and disease. Indeed, antibiotic resistance increasingly compromises the outcome of many infections that were, until recently, treatable and remain the most common diseases in Africa.[3]

The emergence of antibiotic resistance is primarily due to excessive and often unnecessary use of antibiotics in humans and animals.[4] When faced with a patient suffering from serious infection, the choice of antibiotic depends on clinical judgement and a knowledge of the geographic distribution of resistance among bacteria isolated in the hospital and local community.[5] Thus, continuous monitoring of the pattern of bacterial resistance serves as empirical guide for therapy.

This study was done to examine the resistance patterns of organisms isolated from patients to antibiotics used in the treatment of infections in University of Nigeria Teaching Hospital (UNTH), Enugu. The project was divided into three parts:

1 The resistance patterns of the isolates were examined from an overall perspective irrespective of the site of isolation
2. A comparison of the resistance patterns were made between urinary and nonurinary isolates
3. The resistance pattern of urinary isolates from inpatients was compared to that of outpatients.

MATERIALS AND METHODS

The sensitivity of a total of 1,718 bacterial isolates from clinical specimens to 20 antimicrobial drugs was studied in 2002 at the University of Nigeria Teaching Hospital, Enugu. The specimens were classified into two groups: urinary and nonurinary specimens. The nonurinary group included wound swabs, blood, body fluids, specimens from respiratory tract, ear, nose and throat, genital and conjuctival regions. The urinary group was divided into those from inpatients and outpatients.

The organisms selected for the study (numbers tested), which included all the strains isolated throughout the year, were as follows: coliforms (897), *Staphylococcus aureus* (403), streptococcus sp (143), *Pseudomonas aeruginosa* (137), Proteus sp (88) and coagulase-negative staphylococci (50). The coliform group was not differentiated. The organisms were identified by routine laboratory methods. Due to nonavailability of methicillin and vancomycin discs, the number of methicillin-resistant staphylococci (MRSA) and vancomycin-resistant coagulase-negative staphylococci could not be documented. The following antimicrobial agents were included for sensitivity testing: pefloxacine (5 mg), nalidixic acid (30 mg), nitrofurantoin (50 mg), ampicillin (10 mg), cotrimoxazole (25 mg), colistin (10 mg), streptomycin (10 mg), tetracycline (30 mg), cefuroxime (30 mg), gentamycin (10 mg), chloramphenicol (10 mg), erythromycin (5 mg), penicillin (5 IU), cephalexin (30 mg), norfloxacin (5 mg), ofloxacin (5 mg), ceftazidime (30 mg) and ciprofloxacin (5 mg).

Due to the nonavailability of some antimicrobial discs at certain periods, not all antimicrobials were tested against the organisms in equal number. Antibiotic sensitivity testing was performed on sensitivity test agar (Biotec, United Kingdom) using the disc diffusion method in accordance with the National Committee for Clinical Laboratory Standards.[6]

S. aureus (ATCC 29213) and *E. coli* (A 35218) were used for quality control of all tests.

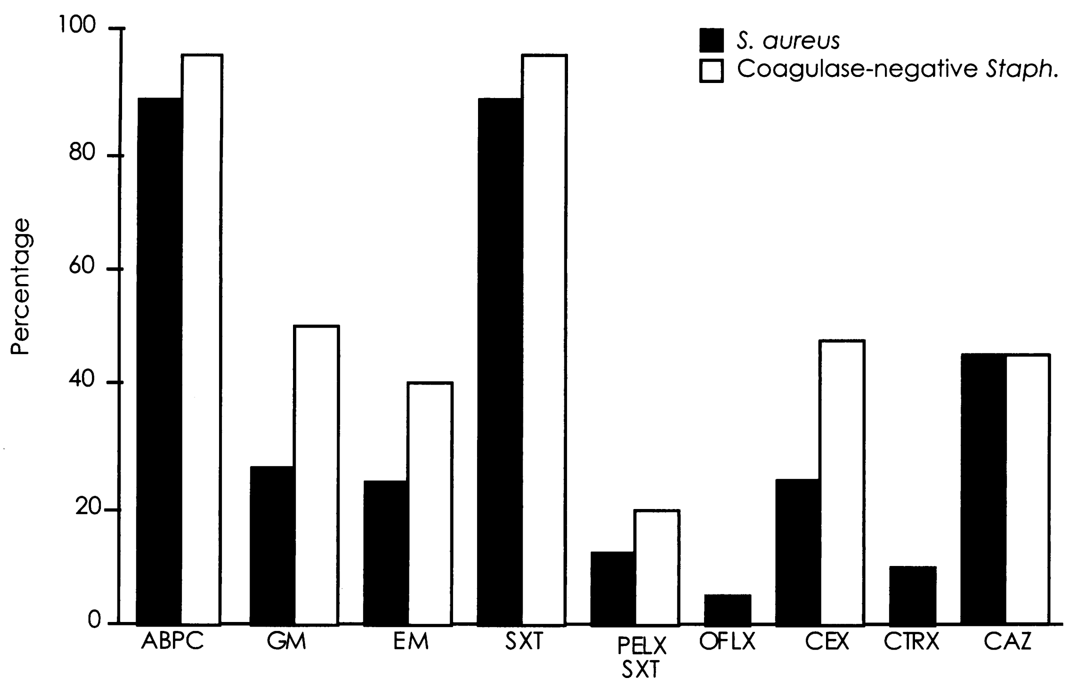
RESULTS

Overall Pattern

A total of 1,718 isolates were studied. Coliforms comprised 897 (52.2% of) isolates and showed high percentage sensitivity to ceftazidime (86.47%), pefloxacine (83.7%) and ciprofloxacin (89.7%), with much reduced sensitivity to ampicillin (19.1%) and cotrimoxazole (11.1%) (Figure 1). *S. aureus* was most sensitive to ciprofloxacin (96.2%), pefloxacine (90.7%) and cephalexin (79.7%) but with much reduced sensitivity to ampicillin (13%) and cotrimoxazole (10.9%). Coagulase-negative staphylococci showed a high degree of resistance to cotrimoxazole (90%), ampicillin (96.7%) and gentamycin (50.3%) (Figure 1).

Out of 137 strains of *P. aeruginosa* studied, on

Figure 1. Resistance of *Staphylococcus* species. Resistance patterns of *S. aureus* and coagulase-negative staphylococcus against ampicillin, gentamycin, erythromycin, cotrimozxazole, pefloxacine, ofloxacin, cephalexin, ceftazidime, and ceftriaxone



ABPC: ampicillin, GM: gentamycin, EM: erythromycin, SXT: cotrimozxazole, PELX: pefloxacine, OFLX: ofloxacin, CEX: cephalexin, CAZ: ceftazidime, CTRX: ceftriaxone the average, 96.3% were resistant to ampicillin and 86.4% to cephalexin (Figure 3). A much lower percentage were resistant to pefloxacine (19.2%), colistin (16.2%) and ceftazidime (21.2%). Proteus species showed lowest resistance to ceftriaxone (13%), norfloxacin (15.1%), ofloxacin (17%) but very high resistance to tetracycline (90%) and colistin (85.3%) (Figure 2).

Comparison of Urinary versus Nonurinary Gram-Negative Bacilli

Similar rates of resistance were observed among urinary and nonurinary isolates of coliforms to most of the antibiotics except ampicillin, gentamycin, colistin and ciprofloxacin, where nonurinary isolates had higher rates of resistance but the rate of gentamycin resistance was higher among urinary than nonurinary isolates.

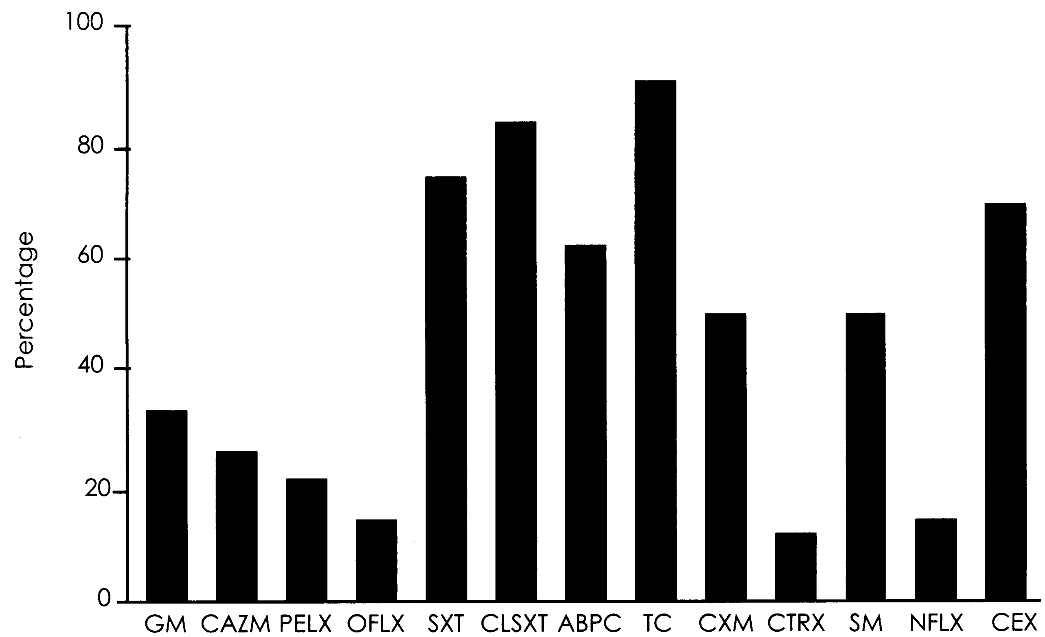
When urinary and nonurinary isolates of *P. aeruginosa* were compared, high rates of resistance was observed among nonurinary isolates of gentamycin and ciprofloxacin, with similar percentages being observed for other drugs. Higher percentage resistance among proteus strains was observed among

Table 1. The resistance in percentages of urinary versus nonurinary coliforms and *P. aeruginosa* against standard drugs

Organism	Source	Antimicrobial Agents			
		ABPC	GM	CL	OFLX
Coliforms	(U)	77.30	44.87	21.03	2.63
	(NU)	84.60	38.38	26.19	21.57
Proteus sp	(U)	5.00	50.00	88.89	13.4
	(NU)	55.6	28.00	87.7	20.6
P. aeruginosa	(U)	100.0	71.05	85.2	20.2
	(NU)	92.6	30.05	87.2	24.2

ABPC: ampicillin, GM: gentamycin, CL: colistin, OFLX: ofloxacin, U: urinary isolates, NU: nonurinary isolates

Figure 2. Resistance patterns of *Proteus sp* against gentamycin, ceftazidime, pefloxacin, ofloxacin, cefuroxime, colistin, ampicillin, tetracycline, cefuroxime, ceftriaxone, streptomycin, corfloxacin, cephalexin and cotrimoxazole



GM: gentamycin, CAZ: ceftazidime, PELX: pefloxacin, OFLX: ofloxacin, CXM: cefuroxime, CL: colistin, ABPC: ampicillin, TC: tetracycline, CXM: cefuroxime, CTRX: ceftriaxone, SM: streptomycin, NFLX: corfloxacin, CEX: cephalexin, SXT: cotrimoxazole nonurinary isolates to cephalexin and cotrimoxazole than for urinary isolates (Figure 3).

Comparison of Inpatient and Outpatient Urinary Coliform Isolates

Antimicrobial resistance by coliform isolates among outpatients was slightly lower to ampicillin (82.4%), gentamycin (52.2%) and ceftazidime (10.4%), compared with 86.0%, 58.06% and 16.66%, respectively, among inpatients. The percentage of resistance was slightly higher to nitrofurantoin and nalidixic acid among inpatients than outpatients.

DISCUSSION

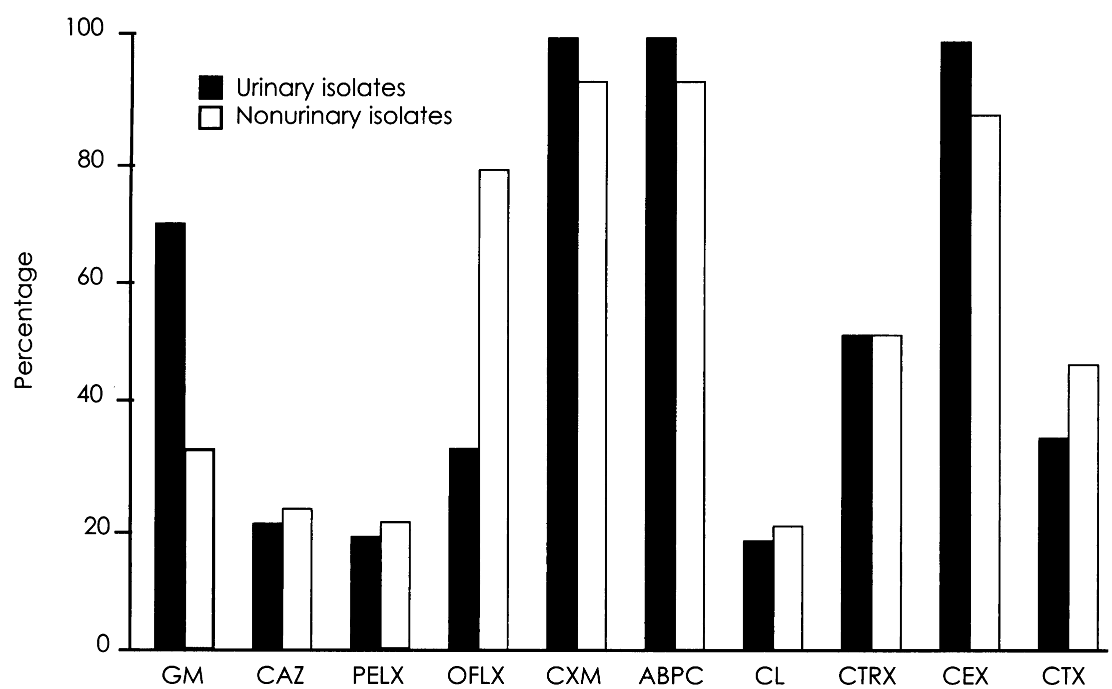
The resistance of bacteria to antibiotics, particularly those used for first-line therapy, is an increasing cause for concern.[7] The continued surveillance of hospital bacteria and their resistance pattern is important in the management of nosocomial infections.[5]

The coliforms isolated in this study showed a high degree of resistance to most drugs tested, with many of them being multidrug resistant. Ampicillin resistance to coliforms in this study was 80.9%, compared to 50% for *E. coli* and 3% for *Klebsiella* in Singapore.[5] The latter authors, however, were able to reduce the resistance of coliforms to aminopenicillin by 28–66.5% by the addition of penicillinase inhibitors—clavullinic acid or sulbactam to ampicillin/amoxicillin. Such a similar reduction in ampicillin resistance could not be confirmed in this study due to the absence of the corresponding discs. Ampicillin is among the most commonly abused and misused drugs in Nigeria. It is commonly available without doctor's prescription, and this obviously is responsible for the high percentage of resistance recorded.

Gentamycin is the only aminoglycoside commonly used in Nigeria. Resistance by coliforms to this antibiotic was 42% in this study compared with 6% for *E. coli* and 30% for *Klebsiella* by others.[5] The high rate of use in our hospital is due to lack of other aminoglycosides, such as amikacin and netilimicin, and this probably accounted for the higher resistance recorded. Fluoroquinolones and cephalosporins performed very satisfactorily against bacterial isolates, compared to other antibiotics apart from the multiantibiotic-resistant strains. This is similar to observations from other centers.[5,8] The treatment of infected people in many parts of Africa, including Nigeria, is challenged by the prohibitive cost of these drugs that places them out of the reach of majority of the patients.

The resistance of *S. aureus* to ampicillin, cotrimoxazole and erythromycin was much higher than results from other centers.[5] These antibiotics are com-

Figure 3. Resistance of *Pseudomonas aeruginosa*. Resistance patterns of urinary versus nonurinary *P. aeruginosa* against gentamycin, ceftazidime, pefloxacin, ofloxacin, cefuroxime, ampicillin, colistin, ceftriaxone, cephalexin and cefotaxime



ABPC: ampicillin, GM: gentamycin, EM: erythromycin, SXT: cotrimozxazole, PELX: pefloxacine, OFLX: ofloxacin, CEX: cephalexin, CAZ: ceftazidime, CTRX: ceftriaxone monly available from unsanctioned providers, and this can lead to subtherapeutic doses being used by these patients. Also, poor-quality drugs that provide subinhibitory selective pressure are commonly available in many parts of Africa, including Nigeria[3], thereby promoting antibiotic resistance.

Due to unavailability of methicillin discs, the prevalence of MRSA infections could not be documented. In contrast, results from other parts of the developed world,[5,8] reveal high prevalence of MRSA, with prevalence of up to 40%. For similar reasons, methicillin and vancomycin resistance among coagulase-negative staphylococci could not be documented but in Singapore[5] vancomycin resistance was absent.

The resistance of the isolates to gentamycin was lower among the nonurinary isolates than the urinary isolates similar to other studies.[5,9,10] With the availability of fluoroquinolones and cephalosporins, there has been a decrease in the use of gentamycin by Nigerian physicians, coupled with the fact that Nigerians generally prefer oral drugs. Most of the urinary isolates were from catheterized patients, many of them on admission, necessitating the use of intravenous gentamycin.

Antimicrobial resistance among isolates from outpatients was lower to ampicillin, gentamycin and ceftazidime compared to inpatients. This is obviously due to the fact that most of the inpatients were catheterized at one period or the other, thus, predisposing to recurrent infections with more antibiotic-resistant organisms. All the outpatient specimens were collected from those attending our hospital clinics and, as has been suggested,[5] this may not truly reflect the susceptibility pattern of community acquired infections.

The emergence of antibiotic resistance is primarily due to excessive and often unnecessary use of antibiotics in humans and animals.[10] Unfortunately, in Nigeria as has equally been observed,[3] much of the antibiotic therapy is not laboratory individualized or even laboratory extrapolated, leading to empirical prescription. Thus, continuous surveillance susceptibility testing is necessary for cost-effective customization of empiric antibiotic therapy. This coupled with the prudent use of antibiotics and infection control, sanitation and hygiene practices will help stem further increase in resistance.[3]

REFERENCES

1. Dennesen PJ, Boten MJ, Weinstein RA. Multi-resistant bacteria as a hospital epidemic problem. *Ann Med.* 1998; 30(2):176-85.

2. McGrowen J Jr, Tenover F. Antimicrobial resistance in the intensive care unit; impact of new patterns. *Int-Clin—Prac-Suppl.* 1998;95:14-22.

3. Okeke I, Sosa A. Antibiotic resistance in Africa: discerning the enemy and plotting a defence. *Africa Health.* 2003;25(3):11-15.

4. Rao GG. Risk factors for the spread of antibiotic resistance bacteria. *Drugs.* 1998;55(3):323-330.

5. Gramim K, Carol C, Koli BL, et al. Antimicrobial resistance problem in a University hospital. *Pathology.* 1995;22:67-70.

6. National Committee for clinical laboratory standards. Performance standards for antimicrobial disc susceptibility tests. 7th ed. Approved standards document M2A7. Wayre, PA, 2000.

7. Johnson AP. Antibiotic resistance among clinically important gram positive bacteria in the UK. *J Hosp Infect.* 1998;40(1):17-26.

8. Dombusch K, King A, Logakia N. Incidence of antibiotic resistance in blood and urine isolates from hospitalized patients. Reports from a European collaborative study. European Study Group on Antibiotic Resistance (ESGAR). *Scand J Infect Dis.* 1998;30(3):281-288.

9. Ozumba UC. Antibiotic resistance of Urinary Pathogens isolated from patients attending University of Nigeria Teaching Hospital (UNTH), Enugu between 1989 and 1993. *Orient J Med.* 2002;14:1-4.

10. Wariso BA, Nwachukwu CO. A survey of common pathogens in wound in patients at the University of Portharcourt Teaching Hospital (UPTH), Portharcourt. *West Afr Med J.* 2003;22(1):50-54. ■